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Nitrosocarbonyl Carbohydrate Derivatives: Hetero Diels–Alder and Ene Reaction Products for Useful Organic Synthesis

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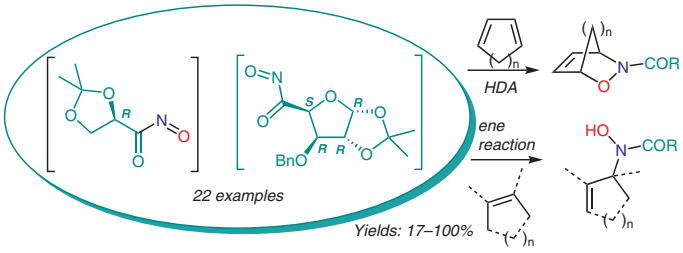

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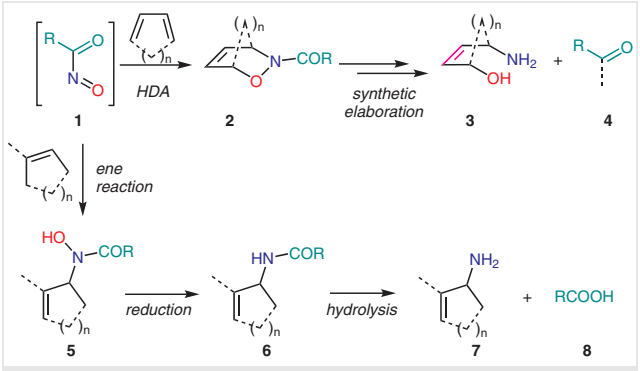
Abstract The generation and trapping of two new nitrosocarbonyl intermediates bearing carbohydrate-based chiral substituents is achieved by the mild oxidation of the corresponding nitrile oxides with tertiary amine *N*-oxides. Their capture with suitable dienes and alkenes afforded the corresponding hetero Diels–Alder cycloadducts and ene adducts from fair to excellent yields. The entire methodology looks highly promising by the easy conversion of aldoximes into hydroxymoyl halides, widening the access to nitrosocarbonyls, versatile tools in organic synthesis.

Key words nitrosocarbonyl, hetero Diels–Alder reactions, ene reactions, nitrile oxides, synthetic applications



Scheme 1 Synthetic utility of nitrosocarbonyl chemistry in HDA and ene reactions

Nitrosocarbonyl intermediates **1** are fleeting and highly reactive species, obtainable from a variety of sources such as hydroxamic acids, *N*-hydroxycarbamates, *N*-hydroxyureas, nitrile oxides, 1,2,4-oxadiazole-4-oxides, and nitrodiazoalkanes.[1] Since nitrosocarbonyls (***NC***) do not survive for long (their stability was determined to be up to 180 μs),[2] trapping with suitable dienes in hetero Diels–Alder (HDA) reactions or with alkenes in ene reactions represents the way to take advantage of these versatile synthetic tools. In spite of their nature of transient species, ***NC*** **1** continue to hold a tremendous amount of synthetic potential as intermediates in the construction of a variety of biologically interesting molecules.[1] Their reactivity is nicely displayed in HDA and ene reactions (Scheme 1). In the first case, the use of a variety of acyclic or cyclic dienes allows for obtaining the corresponding cycloadducts of type **2** that can be easily elaborated into aminols **3** (with loss of the acyl fragment **4**) where valuable functional groups, OH and NH_2, are installed in a *cis* stereochemical relationship on a carbocyclic skeleton.

Moreover, the C=C bond is suitable for further derivatization. Second, the ene reactions can be performed under mild conditions with acyclic or cyclic alkenes to afford the acylhydroxylamines **5** through the construction of a new C–N bond; these products can be easily reduced to the corresponding amides **6**, whose hydrolysis produces new amines of type **7** (allylic amination) along with the carboxylic acids **8**.[1]

However, the ***NC*** role is not, as it seems, restricted to furnish two heteroatoms to be located in different carbon skeletons depending upon the reaction conditions; the R–C=O moieties, when attached to the structures, as in the cases of compounds **2**, **5**, and **6**, play a fundamental role, especially in the definition of the biological properties of the entire molecules.

On pursuing our traditional investigations on the chemical behavior of ***NC***s, we wished to apply our efficient and mild method for the generation of these fleeting intermediates to the nitrile oxides obtained from carbohydrate sources, such as the (*R*)-(2,2-dimethyl-1,3-dioxolan-4-one) (**A**) and the (3a*R*,5*S*,6*R*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetra-

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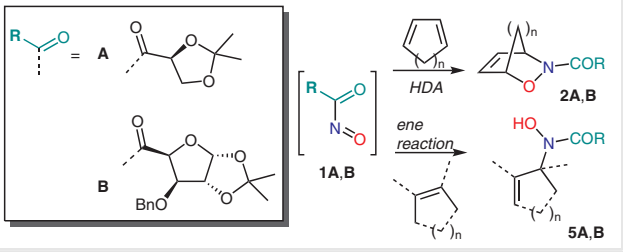
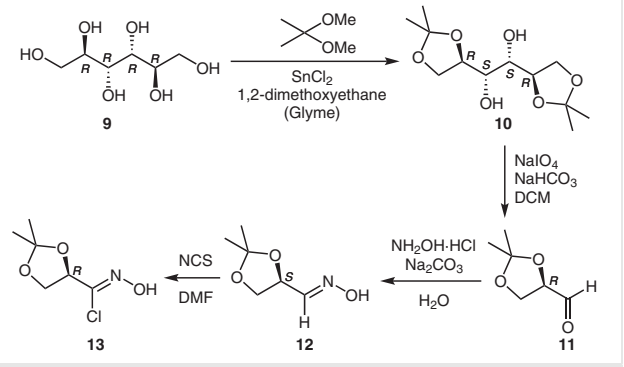


Scheme 2 Synthetic pathway of substituted nitrosocarbonyl intermediates in HDA and ene reactions

hydrofuro [2,3-*d*][1,3]dioxol-5-one (**B**) (see inset in Scheme 2), by the oxidation of the corresponding 1,3-dipoles with tertiary amine *N*-oxides. These structural features are commonly found in several biological active molecules as antivirals and anticancer compounds.[3] For example, derivatives containing the scaffold **A** are typically used to prepare antiviral compounds[3] such as in the Peramivir analogues[4] or can be found in anticancer compounds coupled with cisplatin.[5] β-Glucosidase inhibitors were prepared from the nitrile oxide containing the structure **B** derived from glucose.[6] The intrinsic importance to develop novel compounds with potential biological activities and the desire to verify the applicability of the nitrile oxide oxidation protocol to carbohydrate substituted 1,3-dipoles, prompted us to investigate the HDA and ene reactions of these new in situ generated ***NC*** intermediates.



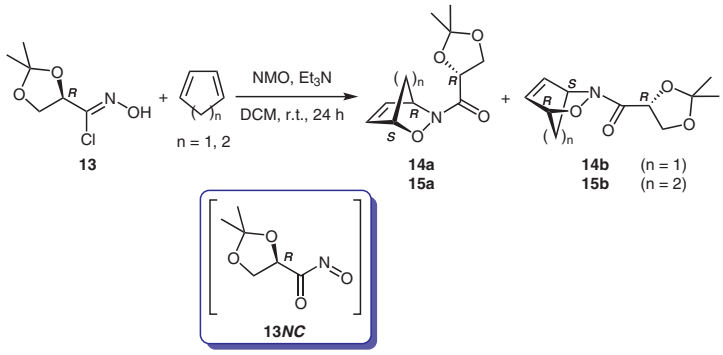
Scheme 3 Synthesis of the (*R*)-*N*-hydroxy-2,2-dimethyl-1,3-dioxolane-4-carbimidoyl chloride (**13**) from D-mannitol (**9**)

We started investigating the chemical behavior of the ***NC*** of type **A** (Scheme 2) containing a single stereogenic center taking advantage of the easy synthetic elaboration of the commercially available D-mannitol (**9**) (Scheme 3). All the reported synthetic steps are well described in literature.[7]

D-Mannitol (**9**) is protected through reaction with 2,2-dimethoxypropane in the presence of $SnCl_2$ as the catalyst to afford the compound **10** in 60% yield.[8] Oxidation of the diol **10** with periodate led to the aldehyde **11** in 63% yield.[8] This latter was easily transformed into the corresponding oxime **12** through classical procedure in excellent yield (97%); typical treatment with NCS allowed to obtain the desired chloroxime **13** in 98% yield.[9] The structures of all the products reported in Scheme 3 were confirmed by spectroscopic analyses and found identical with the characterizations reported in cited literature.[7–9]

The first attempts to generate in situ the nitrosocarbonyl intermediate **13*NC*** from the chloroxime **13** were conducted in the presence of freshly distilled cyclopentadiene or 1,3-cyclohexadiene in HDA cycloadditions. Following the previous and well-established protocol,[10] a DCM solution of **13** was added to a solution of 1.2 equivalents of NMO along with 1.1 equivalents of Et_3N in the presence of 1.5 equivalents of the selected diene in the same anhydrous solvent (Scheme 4).

The reaction mixtures were left at room temperature for 24 hours and subsequently washed with water. The dried organic phases were then evaporated to dryness to leave the crude products that were purified by column chromatography to afford the desired cycloadducts **14a**,**b** and **15a**,**b** in 77% and 70% yield, respectively. The structures of the HDA cycloadducts were attributed on the basis of the corresponding analytical and spectroscopic data. In ^{1}H NMR ($CDCl_3$) spectra of the 2,3-oxazanorbornene moiety of cycloadducts **14a**,**b**, the olefinic protons are found at δ = 6.38 and 6.60 as broad signals while the protected glyceralde-

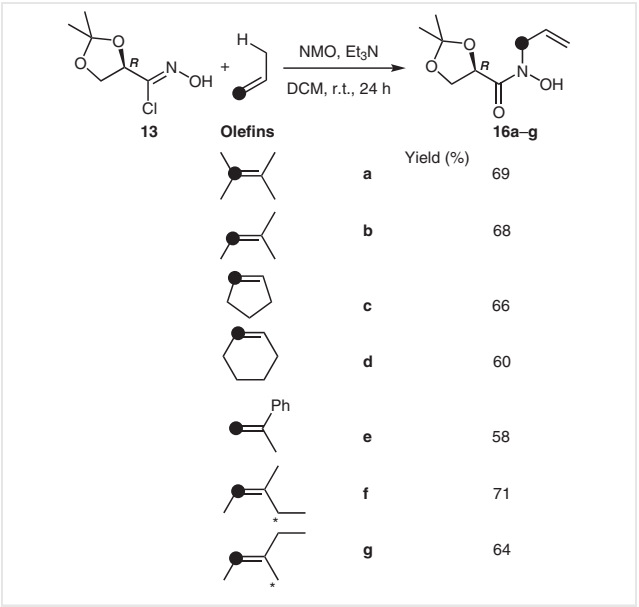


Scheme 4 Synthesis of HDA cycloadducts **14a**,**b** and **15a**,**b** by the mild oxidation of (*R*)-*N*-hydroxy-2,2-dimethyl-1,3-dioxolane-4-carbimidoyl chloride (**13**) with NMO

hyde portion gave three characteristic double doublets at δ = 4.10, 4.28, and 4.71. Similarly, the cycloadducts **15a**,**b** gave in ^{1}H NMR spectra the same distribution of signals in the expected range. The obtained cycloadducts **14a**,**b** and **15a**,**b** are inseparable mixtures of diastereoisomers in the ratio 1.8:1 as shown in particular by the relative heights of the signals in the ^{13}C NMR spectra.

The results above reported indicate the well tolerance of the carbohydrate residue derived from the protected D-mannitol **10** with respect to the oxidative conditions applied to convert the in situ generated nitrile oxide from **13** into the corresponding nitrosocarbonyl intermediate **13*NC***. The chemical yields are very good and no other products were detected in the reaction mixtures with the exception of decomposition products from the highly unstable ***NC***s, as known from the behavior of these fleeting intermediates.[1,11] Any attempt to modify/influence the diastereoisomeric ratio by decreasing the reaction temperature from 0 °C to –40 °C failed, also due to the strong slowdown of the reaction kinetics and subsequent rise of the competitive ***NC*** dimerization/decomposition pathway that renders the desired HDA cycloadducts unobtainable.

More challenging were the ene reaction experiments, since it was known that these reaction are highly dependent upon a fast trapping of the ***NC*** intermediate by the olefinic partner.[12,13] Again, we followed the previously described protocol for these reactions[12,13] by adding a DCM solution of **13** to DCM solutions of 1.2 equivalents NMO along with 1.1 equivalents Et_3N in the presence of 15 equivalents of the selected alkenes **a**–**g** (Scheme 5). The reaction mixtures were left at room temperature for 24 hours and subsequently washed with water. The dried organic phases were then evaporated to dryness to leave the crude products that were purified by column chromatography to afford the desired ene adducts **16a**–**g** in good overall yields (58–71%).



Scheme 5 Synthesis of ene adducts **16a**–**g** by the mild oxidation of (*R*)-*N*-hydroxy-2,2-dimethyl-1,3-dioxolane-4-carbimidoyl chloride (**13**) with NMO. The dot indicates the site of the nitrogen atom attachment of the nitrosocarbonyl moiety and the asterisk in olefins **f** and **g** the site of allylic hydrogen abstraction.

The structures of the ene adducts **16a**–**g** were attributed on the basis of the corresponding analytical and spectroscopic data. The relevant physical chemical and spectroscopic data are shown in Table 1.

It is worth noting that compounds **16b**,**c**,**d**,**f**,**g** were obtained as mixtures of diastereoisomers in nearly 1:1 ratio in all the cases. For compounds **16b**,**d**,**f**,**g**, we were able to separate the two diastereoisomers that were singularly fully characterized while compound **16c** remained as an inseparable mixture and was characterized as it is. Significantly,

Table 1 Physical and Spectroscopic Data of Ene Adducts **16a**–**g**

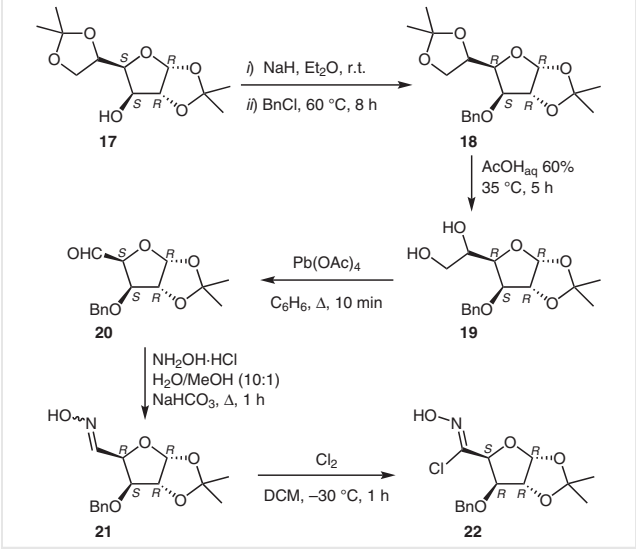
Ene adduct **16**	Mp (°C)[a]	IR (cm^{-1})[b]	^{1}H NMR (DMSO-d_6)		
		$\nu_{C=O}$, ν_{OH}	HC–N	Olefinic Hs	OH
a	179–180	1641, 3092	–	4.76 (s), 4.68 (t)	9.55 (s)
b 1st diast.	90–91	1640, 3092	4.82 (q)	4.87 (s), 4.92 (s)	9.35 (s)
2nd diast.	111–112	1644, 3095	4.85 (m)	4.86 (s), 4.90 (s)	9.46 (s)
c (mix diast.)	121–123	1627, 3179	5.40 (m)	5.56, 6.02 (m)	9.39 (s)
d 1st diast.	99–100	1642, 3059	4.84 (m)	5.46, 5.87 (m)	9.47 (s)
2nd diast.	114–115	1628, 3179	4.85 (m)	5.49, 5.87 (m)	9.46 (s)
e	94–95	1650, 3200	4.56 (m)	5.23, 5.59 (s)	9.80 (s)
f 1st diast.	91–92	1642, 3095	4.79 (m)	5.39 (q)	9.25 (s)
2nd diast.	82–83	1647, 3100	4.80 (m)	5.36 (q)	9.33 (s)
g 1st diast.	116–117	1646, 3098	4.89 (m)	4.93 (s)	9.33 (s)
2nd diast.	121–122	1645, 3097	4.88 (m)	4.92 (s)	9.40 (s)

[a] Colorless crystals from benzene/PE.
[b] Nujol mull.

the use of DMSO-d_6 in proton NMR spectra allowed to evidence the hydroxylamine acidic proton, found in all the cases in the range δ = 9.25–9.80 as singlets. The dioxolane protons were found in the expected region δ = 3.5–5.0 as multiplets. The results illustrated here clearly indicate the excellent tolerance of the applied experimental conditions (NMO, Et_3N, DCM, r.t., 24 h) for the in situ generation of the nitrosocarbonyl intermediate **13*NC***, also in the case of ene reactions that require large excess of olefins to get acceptable yields of the corresponding adducts.

Another important result is that achieved with the stereoisomeric (*Z*)- and (*E*)-3-methyl-2-pentenes **f** and **g** (see Table 1); these stereoisomeric olefins were extensively used in the investigations of ene reactions because they allow for fully defining the stereochemical paths and assessing the intriguing phenomenon known as the '*cis* effect', well-documented both in experimental and theoretical studies.[14] Allylic hydrogens on the more congested side of the alkene are exclusively abstracted, thus resembling singlet oxygen behavior.[15] Similarly to what observed before, the intermediate **13*NC*** follows specifically the Markovnikov (M) path through the addition of the electrophilic nitrogen atom to the less substituted C=C carbon atom and nicely maintain the '*cis*' selectivity by abstracting the allylic hydrogen as indicated in Scheme 5 by the asterisk (*) affording the expected ene adducts **16f** and **16g**. The spectral assignments are fully consistent for the given structures; adduct **16f** is characterized by the presence of three methyl groups as singlets and two methyls as doublets and a single olefinic proton as a multiplet while adduct **16g** has three methyl groups as singlets, one methyl as a doublet, and one ethyl group whose methylene shows diastereotopic protons in the ^1H NMR spectra. This behavior of **13*NC*** is perfectly in keeping with that of the nitrosocarbonyl benzene and in general of nitrosoaromatic compounds.[14–16]

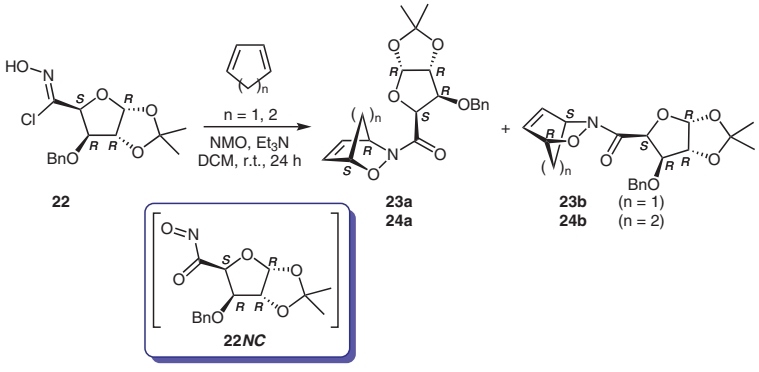
With the aim to further corroborate the ***NC*** generation protocol from sugar-containing residue nitrile oxides, the (3a*R*,5*S*,6*R*,6a*R*)-6-(benzyloxy)-*N*-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole-5-carbimidoyl chloride (**22**) was prepared from the commercially available 1,2,5,6-di-*O*-isopropylidene-α-D-glucofuranose (**17**) (Scheme 6) according to described procedures.[17] Benzyl group protection of **17** afforded compound **18** in 72% yield; this latter was then hydrolyzed to obtain the diol **19** in 87% yield.



Scheme 6 Synthesis of the (3a*R*,5*S*,6*R*,6a*R*)-6-(benzyloxy)-*N*-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole-5-carbimidoyl chloride (**22**) from 1,2,5,6-di-*O*-isopropylidene-α-D-glucofuranose (**17**)

Oxidation[18] of **19** with lead tetraacetate afforded the desired aldehyde **20** in excellent yield (97%), that was converted into the corresponding oxime **21** (yield: 60%, mixture of *syn* and *anti* stereoisomers).[7] Chlorination at –30 °C in DCM solution of **21** gave the desired hydroxymoyl chloride **22** in 74% yield.[19] All the structures of the above reported products were confirmed by spectroscopic analyses and found to be identical with reported data.[17–19]

We first investigated the in situ generation of the nitrosocarbonyl intermediate **22*NC*** from the chloroxime **22** in the presence of freshly distilled cyclopentadiene and 1,3-



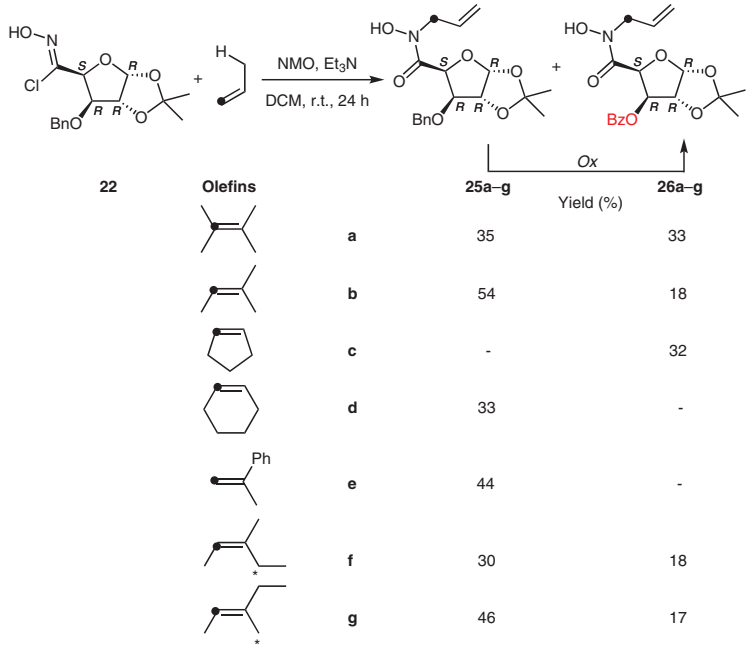
Scheme 7 Synthesis of HDA cycloadducts **23a**,**b** and **24a**,**b** by the mild oxidation of the (3a*R*,5*S*,6*R*,6a*R*)-6-(benzyloxy)-*N*-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole-5-carbimidoyl chloride (**22**) with NMO.

cyclohexadiene, classical conditions to prepare HDA cycloadducts. Following the well-established protocol,[10] a DCM solution of **22** was added to a DCM solution of 1.2 equivalents of NMO along with 1.1 equivalents of Et_3N in the presence of 1.5 equivalents of the selected diene (Scheme 7).

The reaction mixtures were left at room temperature for 24 hours and subsequently washed with water. The dried organic phases were then evaporated to dryness to leave the crude products that were purified by column chromatography to afford the desired cycloadducts **23a**,**b** and **24a**,**b** in 92% and quantitative yield, respectively. The structures of the HDA cycloadducts were attributed on the basis of the corresponding analytical and spectroscopic data. In the ^1H NMR spectra ($CDCl_3$) of the 2,3-oxazanorbornene moiety of cycloadducts **23a**,**b**, the olefinic protons are found at δ = 6.42 and 6.59 as broad singlets. The glucose protected moiety gave the characteristic signals in the range δ = 4.29–5.59. Similarly, the cycloadducts **24a**,**b** gave in ^1H NMR spectra ($CDCl_3$) the same distribution of signals in the expected range. The obtained cycloadducts **23a**,**b** and **24a**,**b** are inseparable mixtures of diastereoisomers in the ratio 1:1 as shown by the relative heights of the ^{13}C NMR signals. These results again confirm the brilliant tolerance of the experimental conditions for the in situ generation of the nitrosocarbonyl intermediate ***22NC*** that was efficiently trapped with the selected dienes affording the HDA cycloadducts in optimum yields. We did not observe any diasteroisomeric preference even by conducting the reaction at lower temperatures.

We completed our investigations on the chemical behavior of ***22NC*** by performing the ene reaction experiments.[12,13] Again, we followed the previous described protocol for these reactions by adding a DCM solution of **22** to DCM solutions of 1.2 equivalents of NMO along with 1.1 equivalents of Et_3N in the presence of 15 equivalents of the selected alkenes **a**–**g** (Scheme 8). The reaction mixtures were left at room temperature for 24 hours and subsequently washed with water. The dried organic phases were then evaporated to dryness to leave the crude products that were purified by column chromatography to afford the ene adducts **25a**,**b**,**d**–**g** and the corresponding oxidized adducts **26a**–**c**,**f**,**g** in fair yields.

Quite surprisingly, the ene reactions of the glucose derivative **22** afforded mixtures of some of the desired compounds of type **25** and some of the adducts **26** where the benzylic methylene was oxidized to the corresponding C=O group. This was confirmed from the spectroscopic analyses; in the ^1H NMR spectra of **26**, the AB system corresponding to the benzylic methylene is absent and in the IR spectra a band in the range 1721–1731 cm^{-1} can now be found. Reasonably, the oxidation is due to the experimental conditions (vide infra). The chemical yields shown in Scheme 8 indicate a variable distribution of the two types of ene adducts; the adducts **25** are somewhat preferred with a single exception (**25c**) while **26d**,**e** are lacking. The sum of the yields of both adducts gives comparable values as those obtained from the same reactions conducted with the chloroxime **13** (see Scheme 5).



Scheme 8 Synthesis of ene adducts **25** and **26** by the mild oxidation of (3a*R*,5*S*,6*R*,6a*R*)-6-(benzyloxy)-*N*-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole-5-carbimidoyl chloride (**22**) with NMO. The dot indicates the site of the nitrogen atom attachment of the nitrosocarbonyl moiety and the asterisk in olefins **f** and **g** the site of allylic hydrogen abstraction.

Table 2 Physical and Spectroscopic Data of Ene Adducts **25a**,**b**,**d–g** and **26a–c**,**f**,**g**

Ene adduct **25**	Mp (°C)[a]	IR (cm^{-1})[b]	^{1}H NMR (DMSO-d_6)		
		$\nu_{C=O}$, ν_{OH}	HC–N	Olefinic Hs	OH
a	184–185	1631, 3140	–	4.73, 4.74 (s)	9.55 (s)
b 1st diast.	175–177	1619, 3110	4.86 (q)	4.91, 4.94 (s)	9.33 (s)
2nd diast.	178–180	1634, 3158	4.85 (m)	4.85 (m)	9.42 (s)
d (mix diast.)	192–194	1639, 3158	4.87 (m)	5.49, 5.91 (m)	9.51 (s)
e	195–196	1624, 3152	4.65 (AB)	5.29, 5.61 (s)	9.86 (s)
f (mix diast.)	180–182	1626, 3149	4.94	4.87, 4.94 (s)	9.34 (s)
g 1st diast.	178–179	1640, 3134	4.92 (q)	4.95 (s)	9.27 (s)
2nd diast.	185–186	1628, 3176	4.95 (q)	4.89, 4.92 (s)	9.36 (s)
Ene Adduct **26**	Mp (°C)[a]	IR (cm^{-1})[b]	^{1}H NMR (DMSO-d_6)		
		$\nu_{C=O}$, ν_{OH}	HC–N	Olefinic Hs	OH
a	208–209	1638, 1721, 3176	–	4.71 (s)	9.71 (s)
b (mix diast.)	200 (dec.)	1635, 1731, 3170	4.83 (q)	4.85, 4.93 (s)	9.49 (s)
c (mix diast.)	225 (dec.)	1635, 1725, 3164	5.39 (m)	5.83, 5.99 (s)	9.57 (s)
f (mix diast.)	209–210	1632, 1724, 3086	4.80 (q)	5.35 (q)	9.36 (s)
g (mix diast.)	196–197	1637, 1725, 3116	4.94 (q)	4.89, 4.92 (s)	9.43 (s)

[a] Colorless crystals from benzene/PE.
[b] Nujol mull.

The structures of the ene adducts **25a**,**b**,**d–g** and the corresponding oxidized adducts **26a–c**,**f**,**g** were attributed on the basis of the corresponding analytical and spectroscopic data and the relevant information are gathered in Table 2 along with their physical data.

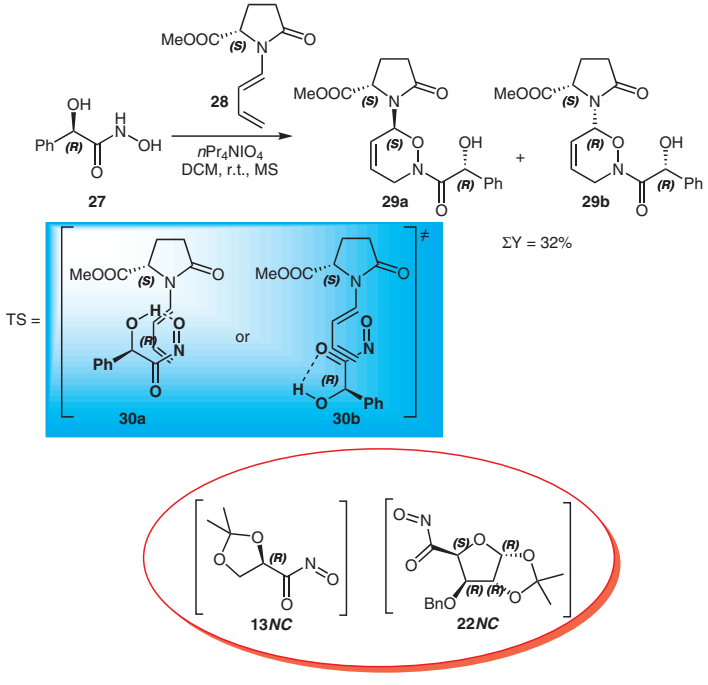
Adducts **25b**,**d**,**f**,**g** as well as **26b**,**c**,**f**,**g** were obtained as mixtures of diastereoisomers in nearly 1:1 ratio with the exception of **25d** (dr, 1.4:1), **26b** (dr, 5:1), **26c** (dr, 4.3:1), and **26g** (dr, 9.5:1). These data are, however, too random to describe a specific diastereoselection. For compounds **25b**,**g** we were able to separate the two diastereoisomers that were singularly fully characterized. The diagnostic hydroxylamine acidic proton signals were found in all the cases in the range δ = 9.27–9.86 as singlets. The protected glucose portion of the molecules gave the expected signals, found in the region δ = 4.2–6.0. The experimental conditions somewhat affect the chemical outcome of the ene reactions as previously accounted with partial oxidation of the benzylic methylene of some of the ene adducts. Reasonably, due to the extremely short life-time of the ***NC*** intermediates in general (**22*NC*** does not escape this behavior) it is difficult to believe that the oxidation can occur at the ***NC*** generation step; more probably it occurs on the final ene adducts and not in all the cases in the same manner. Nevertheless the chemical yields are good if we consider the sum of both types of adducts and somewhat comparable with those of compounds **16**.

Similarly to what was described above for compounds **16**, the ene reactions in the presence of the stereoisomeric (*Z*)- and (*E*)-3-methyl-2-pentenes **f** and **g** (see Table 2) allowed for defining the stereochemical paths and again assessing the '*cis* effect'.[14] Allylic hydrogens of (*Z*)- and (*E*)-3-methyl-2-pentenes **f** and **g** were abstracted on the more congested side of the alkene.[15] Intermediate **22*NC*** follows specifically the M path through the addition of the electrophilic nitrogen atom to the less substituted C=C carbon atom and nicely maintain the '*cis*' selectivity as indicated in Scheme 8 by the asterisk (*) affording the expected ene adducts. The structures of adducts **25f**,**g** and **26f**,**g** are fully consistent with their spectral data analogously with the previous observations. This behavior of **22*NC*** is perfectly in keeping with that of the nitrosocarbonyl benzene and in general of nitrosoaromatic compounds.[14–16]

We have investigated the ***NC*** generation protocol applied to nitrile oxides bearing chiral substituents prepared from carbohydrate sources. For these 'proof of concept' studies we decided to install on the nitrile oxide moiety (i.e., on the corresponding hydroxymoyl chlorides **13** and **22**) two substituents of different complexity easily prepared from commercially available D-mannitol (**9**) and 1,2,5,6-di-*O*-isopropylidene-α-D-glucofuranose (**17**), following the well-described literature procedures.[7–9,17–19] The aim was to verify the compatibility of the oxidative conditions of the in situ generated nitrile oxides with the maintenance of the nitrosocarbonyl structure in view of their trapping with dienes or alkenes to get a variety of HDA and ene adducts. In fact, by inserting carbohydrate substituents on the CO–NO moiety, it was not obvious or predictable a chemical behavior in full agreement with that of aliphatic or aromatic nitrosocarbonyl intermediates.[10] The fast di-

merization route that nitrosocarbonyl could be a detrimental and strongly competitive pathway determining a failure of the investigations at hand.[11,20] A second task was to verify the resistance of the carbohydrate protections under the experimental conditions. In this field, the results were substantially positive: totally in the case of the reactions with hydroxymoyl chloride **13** and in part with compound **22**. A brief comment to the chemical yields can be done regarding the results obtained for the adducts **26c** and **25d**; the low yields are not surprising since we have demonstrated that cyclopentene and cyclohexene are at the end of the reactivity scale, four time less reactive than trisubstituted olefins.[13] In this latter case, the presence of the benzylic moiety as protecting group containing a highly reactive methylene[21] led to the isolation of the oxidized ene adducts **26** bearing a benzoyl group, reasonably from the oxidation of the corresponding benzyl protected adducts **25**. The oxidation of the benzylic methylene seems to occur by means of the excess NMO or, maybe, by other oxidants generated in solution. Control experiments conducted on some adducts of type **25** in the presence of excess NMO both at room temperature and upon heating did not lead to the corresponding oxidized compounds **26**. Hence, the reason for the oxidation of the benzylic methylene has to be ascribed to other species formed during the ***NC*** generation. It remains surprisingly and difficult to explain the occurrence of this behavior in the ene reaction only. Lastly, we aimed to verify the possibility to have a chirality induction effect on the diastereoisomeric ratio of both HDA and ene adducts, wherever applicable. This final task failed even by changing the experimental conditions by decreasing the reaction temperature to favor a more rigid approach between the addends in HDA cycloaddition reactions and in the ene additions. Unfortunately, nitrosocarbonyl fleeting intermediates, surviving for 180 μs only,[2] are hardly manageable from this point of view.

The key point for discussing the asymmetric induction can be easily illustrated by the reaction shown in Scheme 9. The chiral hydroxamic acid **27** is oxidized under classical conditions by means of tetrapropylammonium periodate to afford the corresponding nitrosocarbonyl intermediate that is trapped by a chiral diene **28** to give the expected HDA cycloadducts **29a**,**b** in 32% overall yield.[22] In spite of the low chemical yields, the possibility for the hydroxamic acid **27** to form an intramolecular hydrogen bond surviving after the oxidation to ***NC*** as well as the stereochemical constraints imposed by the chiral diene build the correct transition structures (TS) **30a** or **30b**, which are responsible for the asymmetric induction. These features are lacking in our tested intermediates **13*NC*** and **22*NC***. Many examples can be found in literature and the hydroxamic acids are used exclusively for the generation of chiral ***NC***s and in a good number of cases chiral dienes are also contributing in the final result.[1] No examples are found in the case of nitrile oxides; these results are indeed the first examples reported in literature although not leading to any stereopreference.



Scheme 9 Double asymmetric induction with chiral nitrosocarbonyl **27** and chiral diene **28**

On the basis of the above reported comments, the main positive outcome of the illustrated results is the possibility to elaborate synthetically carbohydrate compounds to access different aldehyde derivatives that can easily converted into the corresponding oximes as precursors of the nitrile oxides needed for the ***NC*** intermediate generation by taking advantage of the mild and efficient protocol described in the present work. The efficiency is quite remarkable since it is worth noting that the HDA and ene adducts were the only products observed with no dimerization of the corresponding nitrile oxide to the furoxans or with a limited decomposition by dimerization of the nitrosocarbonyl intermediates under the applied experimental conditions.

This opportunity has an intrinsic value from the synthetic point of view since several structures of biological active molecules contain the prepared scaffolds, in an identical form or slight modified, as shown in two examples **I** (2-{4-[(4*R*,5*R*)-5-benzo[*d*]thiazole-2-carbonyl-2,2-dimethyl-1,3-dioxolane-4-carbonyl]piperazin-1-yl}benzonitrile)[23] and **II** {ethyl 5-(3-ethoxy-3-oxoprop-1-yn-1yl)-1-[(3a*R*,4*R*,6*R*,6a*R*)-6-(hydroxymethyl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl]-1*H*-1,2,3-triazole-4-carboxylate}[24] in Figure 1. Two different heterocyclic compounds can behave as inhibitor of HRV 3C protease or cell death inductor by caspase and in both structures the nitrosocarbonyl substituents can be easily recognized.

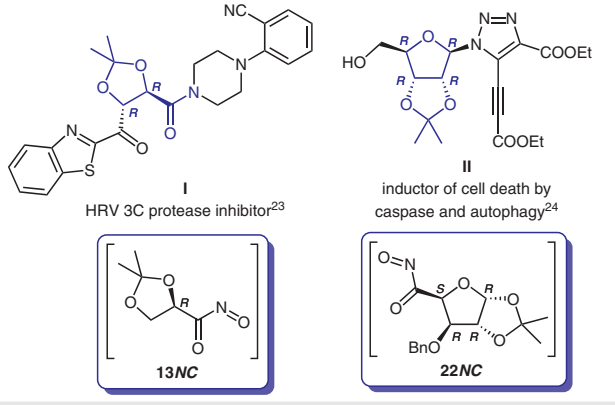


Figure 1 Structures of two biological active compounds having common structural features with chiral nitrosocarbonyls **13*NC*** and **22*NC***

In conclusion, we have reported the generation and trapping of two new nitrosocarbonyl intermediates bearing carbohydrate-based chiral substituents by the mild oxidation of nitrile oxides with tertiary amine *N*-oxides. Their capture with suitable dienes and alkenes afforded the corresponding HDA cycloadducts and ene adducts from fair to excellent yields. The entire methodology looks highly promising by the easy conversion of aldoximes to hydroxymoyl halides, widening the access to a wider and wider array of nitrosocarbonyls, versatile tools in organic synthesis.

All melting points are uncorrected. Elemental analyses were carried out in-house. ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer (solvents specified). Chemical shifts are expressed in ppm from internal TMS (δ) and coupling constants (*J*) are in hertz (Hz). Standard abbreviations were used for defining signal multiplicities. Minor diastereoisomer signals are shown in square brackets when applicable. IR spectra were collected on samples prepared as Nujol mulls and absorptions (ν) are in cm^{-1}. Column chromatography and TLC: silica gel H60 and GF_{254}, respectively; eluents: cyclohexane/EtOAc (9:1) to pure EtOAc.

When diastereosomeric mixtures are obtained, yields near the single stereisomers indicate the sum of both compounds.

D-Mannitol (**9**) and 1,2,5,6-di-*O*-isopropylidene-α-D-glucofuranose (**17**) were purchased from chemical suppliers.[7–9,17–19] Cyclopentadiene was used freshly distilled and 1,3-cyclohexadiene was purchased and used as it is. Alkenes **a**–**g** were purchased from chemical suppliers and used as they are. Other reagents and solvents were purchased from chemical suppliers and used without any further purification.

Compounds **10**–**13** were prepared according the established procedures,[7–9] and their structures were confirmed by comparison with the reported spectroscopic data. Analogously, compounds **18**–**22** were prepared according the established procedures,[17–19] and their structures were confirmed by comparison with the reported spectroscopic data.

HDA Cycloaddition Reactions of (*R*)-*N*-Hydroxy-2,2-dimethyl-1,3-dioxolane-4-carbimidoyl Chloride (13) with Cyclopentadiene and 1,3-Cyclohexadiene; General Procedure

A DCM solution (50 mL) of **13** (1.80 g, 10 mmol, 1 equiv) was added to a DCM solution (100 mL) of NMO (1.41 g, 12 mmol, 1.2 equiv) along with Et_3N (1.11 g, 11 mmol, 1.1 equiv) in the presence of the selected diene (15 mmol, 1.5 equiv). The reaction mixtures were left at r.t. for 24 h and subsequently washed with H_2O (2 × 30 mL). The dried organic phases were then evaporated to dryness to leave the crude products that were purified by column chromatography to afford the desired cycloadducts **14a**,**b** and **15a**,**b**.

2-Oxa-3-azabicyclo[2.2.1]hept-5-en-3-yl-[(*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]methanone (14a,b)

Yield: 1.73 g (77%); white crystals (benzene/PE); mp 74–75 °C.

IR (Nujol): 1681 (C=O) cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.60 (br s, 1 H, =CH), 6.38 (br s, 1 H, =CH), 5.40 (br s, 1 H, CHO), 5.32 (br s, 1 H, CHN), 4.71 (t, *J* = 7 Hz, 1 H, CHO), 4.28 (t, *J* = 7 Hz, 1 H, CHO), 4.10 (m, 1 H, CHO), 2.01 and 1.80 (m, 1 H + 1 H, CH_2), 1.49 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 170.4 (C=O), 132.7, 132.4, 131.6, 131.2 (CH=CH), 72.1, [71.9], 70.4, [69.7], 65.9, [64.0], 62.7 (OCO, CHO, CHN), 30.8, 25.6 (CH_2), 23.5, [23.0], 20.6, [20.5] (CH_3).

Anal. Calcd for $C_{11}H_{15}NO_4$ (225.24): C, 58.66; H, 6.71; N, 6.22. Found: C, 58.65; H, 6.70; N, 6.24.

2-Oxa-3-azabicyclo[2.2.2]oct-5-en-3-yl-[(*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]methanone (15a,b)

Yield: 1.67 g (70%); white crystals (benzene/PE); mp 84–85 °C.

IR (Nujol): 1688 (C=O) cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.66 (m, 1 H, =CH), 5.50 (m, 1 H, =CH), 5.22 (s, 1 H, CHO), 4.80 (s, 1 H, CHN), 4.61 (t, *J* = 7 Hz, 1 H, CHO), 4.27 (t, *J* = 7 Hz, 1 H, CHO), 4.00 (dd, *J* = 7 Hz, 1 H, CHO), 2.12 (m, 4 H, CH_2CH_2), 1.50 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 170.4, [168.8] (C=O), 132.7, [132.4], [131.6], 131.2 (CH=CH), 72.2, [72.1], 70.4, [69.7] (CHO, CHN), 64.0, [62.7] (CH_2O), 47.4, [47.2], 30.8, [25.6] (CH_2), 23.3, [23.0], 21.1, [20.6] (CH_3).

Anal. Calcd for $C_{12}H_{17}NO_4$ (239.27): C, 60.24; H, 7.16; N, 5.85. Found: C, 60.25; H, 7.19; N, 5.84.

Ene Reactions of (*R*)-*N*-Hydroxy-2,2-dimethyl-1,3-dioxolane-4-carbimidoyl Chloride (13) with Olefins a–g; General Procedure

To a DCM solution (100 mL) of the corresponding olefin **a–g** (15 mmol, 15 equiv) were added NMO (1.41 g, 12 mmol, 1.2 equiv) and distilled Et_3N (1.11 g, 11 mmol, 1.1 equiv). (*R*)-*N*-Hydroxy-2,2-dimethyl-1,3-dioxolane-4-carbimidoyl chloride (**13**; 1.80 g, 10 mmol, 1 equiv) was then dissolved in DCM (50 mL) and the solution was added dropwise to the olefin solutions under stirring at r.t. The reaction mixtures were left to react for 24 h. After this period of time, the mixtures were washed with H_2O (2 × 30 mL) and the organic phases were dried (anhyd Na_2SO_4). The residues obtained after the solvent evaporation were submitted to chromatographic separation for isolation and purification of the products.

(*R*)-*N*-(2,3-Dimethylbut-3-en-2-yl)-*N*-hydroxy-2,2-dimethyl-1,3-dioxolane-4-carboxamide (16a)

Yield: 1.68 g (69%); white crystals (benzene/PE); mp 179–180 °C.

IR (Nujol): 3092, 1641 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.55 (s, 1 H, OH), 4.83 (dd, *J* = 7, 6 Hz, 1 H, CHO), 4.76 and 4.68 (s + t, *J* = 1 Hz, 1 H + 1 H, $=CH_2$), 4.21 and 3.82 (dd, *J* = 9, 7 Hz, 1 H + 1 H, CH_2O), 1.66 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 170.5 (C=O), 149.3 (C=), 109.4 (CH_2=), 108.3 (OCO), 73.8, 64.8 (CHO, CHN), 66.7 (CH_2O), 25.7, 25.6, 25.1, 24.7, 19.0 (CH_3).

Anal. Calcd for $C_{12}H_{21}NO_4$ (243.30): C, 59.24; H, 8.70; N, 5.76. Found: C, 59.25; H, 8.70; N, 5.74.

(4*R*)-*N*-Hydroxy-2,2-dimethyl-*N*-(3-methylbut-3-en-2-yl)-1,3-dioxolane-4-carboxamide (16b), 1st Diastereoisomer

Yield: 1.56 g (68%); white crystals (benzene/PE); mp 90–91 °C.

IR (Nujol): 3092 (O–H), 1640 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.35 (s, 1 H, OH), 4.87 and 4.92 (s, 1 H + 1 H, $=CH_2$), 4.91 (m, 1 H, CHO), 4.82 (q, *J* = 7 Hz, 1 H, CHN), 4.21 and 3.86 (dd, *J* = 8, 6 Hz, 2 H, CH_2O), 1.67 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.21 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 170.4 (C=O), 143.7 (C=), 112.2 ($=CH_2$), 109.6 (OCO), 72.8 (CHO), 66.7 (CH_2O), 54.5 (CHN), 25.8, 25.6, 20.5, 14.8 (CH_3).

Anal. Calcd for $C_{11}H_{19}NO_4$ (229.28): C, 57.63; H, 8.35; N, 6.11. Found: C, 57.64; H, 8.34; N, 6.10.

(4*R*)-*N*-Hydroxy-2,2-dimethyl-*N*-(3-methylbut-3-en-2-yl)-1,3-dioxolane-4-carboxamide (16b), 2nd Diastereoisomer

Yield: 1.56 g (68%); white crystals (benzene/PE); mp 111–112 °C.

IR (Nujol): 3095 (O–H), 1644 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.46 (s, 1 H, OH), 4.90 and 4.86 (s, 1 H + 1 H, $=CH_2$), 4.85 (m, 1 H + 1 H, CHN, CHO), 4.24 (t, *J* = 7 Hz, 1 H, CHO), 3.85 (dd, *J* =7 Hz, 1 H, CH_2O), 1.64 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.22 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 169.7 (C=O), 144.0 (C=), 112.1 ($=CH_2$), 109.6 (OCO), 72.9 (CHO), 66.8 (CH_2O), 54.3 (CHN), 25.7, 25.6, 20.4, 14.8 (CH_3).

Anal. Calcd for $C_{11}H_{19}NO_4$ (229.28): C, 57.63; H, 8.35; N, 6.11. Found: C, 57.65; H, 8.31; N, 6.11.

(4*R*)-*N*-(Cyclopent-2-en-1-yl)-*N*-hydroxy-2,2-dimethyl-1,3-dioxolane-4-carboxamide (16c), Mixture of Diastereoisomers

Yield: 1.50 g (66%); white crystals (benzene/PE); mp 121–123 °C.

IR (Nujol): 3179 (O–H), 1627 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.39 (s, 1 H, OH), 6.02 and 5.56 (m, 1 H + 1 H, CH=CH), 5.40 (m, 1 H, CHN), 4.85 (m, 1 H, CHO), 4.20 and 3.85 (m, 2 H, CH_2O), 2.5–1.7 (m, 4 H, CH_2), 1.37 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 170.1 (C=O), 135.4, [135.2], 129.1, [128.8] (CH=CH), 109.6, [109.5] (OCO), 73.0, [72.9], 66.8, [66.7], (CH_2O), 61.6 (CHN), 31.3, 25.9, 25.8, 25.6 (CH_2, CH_3).

Anal. Calcd for $C_{11}H_{17}NO_4$ (227.26): C, 58.14; H, 7.54; N, 6.16. Found: C, 58.15; H, 7.51; N, 6.16.

(4*R*)-*N*-(Cyclohex-2-en-1-yl)-*N*-hydroxy-2,2-dimethyl-1,3-dioxolane-4-carboxamide (16d), 1st Diastereoisomer

Yield: 1.45 g (60%); white crystals (benzene/PE); mp 99–100 °C.

IR (Nujol): 3059 (O–H), 1642 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.47 (s, 1 H, OH), 5.87 and 5.46 (m, 1 H + 1 H, CH=CH), 4.88 (dd, *J* = 8, 6 Hz, 1 H, CHO), 4.84 (m, 1 H, CHN), 4.21 and 3.88 (m, 2 H, CH_2O), 2.1–1.5 (m, 6 H, CH_2), 1.37 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 170.4 (C=O), 130.8, 127.3 (CH=CH), 109.6 (OCO), 72.9 (CHO), 66.9 (CH_2O), 51.9 (CHN), 25.8, 25.6, 25.1, 23.9, 20.6 (CH_2 and CH_3).

Anal. Calcd for $C_{12}H_{19}NO_4$ (241.29): C, 59.73; H, 7.94; N, 5.81. Found: C, 59.75; H, 7.93; N, 5.82.

(4*R*)-*N*-(Cyclohex-2-en-1-yl)-*N*-hydroxy-2,2-dimethyl-1,3-dioxolane-4-carboxamide (16d), 2nd Diastereoisomer

Yield: 1.45 g (60%); white crystals (benzene/PE); mp 114–115 °C.

IR (Nujol): 3179 (O–H), 1628 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.46 (s, 1 H, OH), 5.87 and 5.49 (m, 1 H + 1 H, CH=CH), 4.88 (dd, *J* = 8, 6 Hz, 1 H, CHO), 4.85 (m, 1 H, CHN), 4.21 and 3.84 (m, 2 H, CH_2O), 2.0–1.5 (m, 6 H, CH_2), 1.37 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 170.5 (C=O), 131.0, 126.9 (CH=CH), 109.6 (OCO), 72.9 (CHO), 66.8 (CH_2O), 52.0 (CHN), 25.8, 25.6, 25.2, 23.9, 20.6 (CH_2 and CH_3).

Anal. Calcd for $C_{12}H_{19}NO_4$ (241.29): C, 59.73; H, 7.94; N, 5.81. Found: C, 59.72; H, 7.94; N, 5.80.

(*R*)-*N*-Hydroxy-2,2-dimethyl-*N*-(2-phenylallyl)-1,3-dioxolane-4-carboxamide (16e)

Yield: 1.61 g (58%); white crystals (benzene/PE); mp 94–95 °C.

IR (Nujol): 3200 (O–H), 1650 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.80 (s, 1 H, OH), 7.48 (m, 2 H_{arom}), 7.30 (m, 3 H_{arom}), 5.59 and 5.23 (s, 1 H + 1 H, $=CH_2$), 4.88 (dd, *J* = 8, 6 Hz, 1 H, CHO), 4.56 (AB syst, 2 H, CH_2N), 4.15 and 3.69 (m, 2 H, CH_2O), 1.35 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 170.0 (C=O), 141.7 (C=), 137.8, 128.3, 127.8, 125.8 (arom), 115.1 (=CH_2), 109.7 (OCO), 72.7 (CHO), 66.6 (CH_2O), 51.2 (CH_2N), 25.7, 25.6 (CH_3).

Anal. Calcd for $C_{15}H_{19}NO_4$ (277.32): C, 64.97; H, 6.91; N, 5.05. Found: C, 64.99; H, 6.90; N, 5.01.

(4*R*)-*N*-Hydroxy-2,2-dimethyl-*N*-[(*E*)-3-methylpent-3-en-2-yl]-1,3-dioxolane-4-carboxamide (16f), 1st Diastereoisomer

Yield: 1.73 g (71%); white crystals (benzene/PE); mp 91–92 °C.

IR (Nujol): 3095 (O–H), 1642 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.25 (s, 1 H, OH), 5.39 (q, *J* = 3 Hz, 1 H, C=CH), 4.89 (t, *J* = 3 Hz, 1 H, CHO), 4.79 (m, H, CHN), 4.20 (t, *J* = 7 Hz, 1 H, CHO), 3.85 (m, 1 H, CHO), 1.58 (d, *J* = 7 Hz, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3), 1.18 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 170.1 (C=O), 134.1 (C=), 120.0 (=CH), 109.6 (OCO), 72.8 (CHO), 66.7 (CH_2O), 55.7 (CHN), 25.8, 25.6, 14.7, 14.1, 13.2 (CH_3).

Anal. Calcd for $C_{12}H_{21}NO_4$ (243.30): C, 59.24; H, 8.70; N, 5.76. Found: C, 59.26; H, 8.70; N, 5.73.

(4*R*)-*N*-Hydroxy-2,2-dimethyl-*N*-[(*E*)-3-methylpent-3-en-2-yl]-1,3-dioxolane-4-carboxamide (16f), 2nd Diastereoisomer

Yield: 1.73 g (71%); white crystals (benzene/PE); mp 82–83 °C.

IR (Nujol): 3100 (O–H), 1647 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.33 (s, 1 H, OH), 5.36 (q, *J* = 3 Hz, 1 H, C=CH), 4.88 (dd, *J* = 8, 6 Hz, 1 H, CHO), 4.80 (m, 1 H, CHN), 4.23 (dd, *J* = 9, 7 Hz, 1 H, CHO), 3.83 (dd, *J* = 8, 7 Hz, 1 H, CHO), 1.58 (d, *J* = 7 Hz, 3 H, CH_3), 1.51 (s, 3 H , CH_3), 1.36 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.19 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 169.6 (C=O), 134.4 (C=), 119.9 (=CH), 109.6 (OCO), 72.9 (CHO), 66.8 (CH_2O), 55.4 (CHN), 25.7, 25.6, 14.8, 14.0, 13.2 (CH_3).

Anal. Calcd for $C_{12}H_{21}NO_4$ (243.30): C, 59.24; H, 8.70; N, 5.76. Found: C, 59.23; H, 8.71; N, 5.77.

(4*R*)-*N*-Hydroxy-2,2-dimethyl-*N*-(3-methylenepentan-2-yl)-1,3-dioxolane-4-carboxamide (16g), 1st Diastereoisomer

Yield: 1.56 g (64%); white crystals (benzene/PE); mp 116–117 °C.

IR (Nujol): 3098 (O–H), 1646 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.33 (s, 1 H, OH), 4.93 (s, 2 H, =CH_2), 4.89 (m, 1 H + 1 H, CHO, CHN), 4.21 (t, *J* = 8 Hz, 1 H, CHO), 3.86 (m, 1 H, CHO), 1.99 (m, 2 H, CH_2), 1.37 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3), 1.21 (d, *J* = 6 Hz, 3 H, CH_3), 0.98 (t, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 170.3 (C=O), 149.0 (C=), 110.2 (=CH_2), 109.6 (OCO), 72.8 (CHO), 66.7 (CH_2O), 53.1 (CHN), 26.2, 25.8, 25.6, 14.9, 12.0 (CH_2 and CH_3).

Anal. Calcd for $C_{12}H_{21}NO_4$ (243.30): C, 59.24; H, 8.70; N, 5.76. Found: C, 59.25; H, 8.71; N, 5.73.

(4*R*)-*N*-Hydroxy-2,2-dimethyl-*N*-(3-methylenepentan-2-yl)-1,3-dioxolane-4-carboxamide (16g), 2nd Diastereoisomer

Yield: 1.56 g (64%); white crystals (benzene/PE); mp 121–122 °C.

IR (Nujol): 3097 (O–H), 1645 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.40 (br s, 1 H, OH), 4.92 (s, 2 H, =CH_2), 4.88 (m, 1 H + 1 H, CHO, CHN), 4.23 (t, *J* = 8 Hz, 1 H, CHO), 3.83 (m, 1 H, CHO), 1.95 (m, 2 H, CH_2), 1.36 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.23 (d, *J* = 6 Hz, 3 H, CH_3), 0.97 (t, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 169.7 (C=O), 149.4 (C=), 109.9 (=CH_2), 109.6 (OCO), 72.9 (CHO), 66.8 (CH_2O), 53.0 (CHN), 26.1, 25.7, 25.6, 15.0, 12.0 (CH_2 and CH_3).

Anal. Calcd for $C_{12}H_{21}NO_4$ (243.30): C, 59.24; H, 8.70; N, 5.76. Found: C, 59.24; H, 8.72; N, 5.74.

HDA Cycloaddition Reactions of (3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole-5-carbimidoyl Chloride (22) with Cyclopentadiene and 1,3-Cyclohexadiene; General Procedure

A DCM solution (80 mL) of **22** (3.28 g, 10 mmol, 1 equiv) was added to a DCM solution (150 mL) of NMO (1.41 g, 12 mmol, 1.2 equiv) along with Et_3N (1.11 g, 11 mmol, 1.1 equiv) in the presence of the selected diene (15 mmol, 1.5 equiv). The reaction mixtures were left at r.t. for 24 h and subsequently washed with H_2O (2 × 50 mL). The dried organic phases were then evaporated to dryness to leave the crude products that were purified by column chromatography to afford the desired cycloadducts **23a**,**b** and **24a**,**b**.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl-2-oxa-3-azabicyclo[2.2.1]hept-5-en-3-ylmethanone (23a,b)

Yield: 3.44 g (92%); white crystals (benzene/PE); mp 143–144 °C.

IR (Nujol): 1692 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 7.30 (m, 5 H_{arom}), 6.59 and 6.42 (br s, 1 H + 1 H, CH=CH), 5.59 (br s, 1 H, OCHO), 5.49 (br s, 1 H, CHO), 5.32 (br s, 1 H, CHN), 4.78 (d, *J* = 2 Hz, 1 H, CHO), 4.70 and 4.50 (AB syst, 1 H + 1 H, CH_2Ph), 4.50 (1 H, CHO), 4.29 (d, *J* = 2 Hz, 1 H, CHO), 1.75 (br, 2 H, CH_2), 1.40 (s, 3 H, CH_3), 1.25 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 169.7 [164.9] (C=O), 137.1, 135.9, 132.4, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.5, 127.4 (arom), 112.4, 112.2, 105.7, 105.5 (CH=CH), 105.3 (OCO), 82.7, 82.5, 82.0, 80.3, 75.1, 72.1 (CHO, CHN), 48.3, (CH_2), 26.8, 26.2 (CH_3).

Anal. Calcd for $C_{20}H_{23}NO_6$ (373.41): C, 64.33; H, 6.21; N, 3.75. Found: C, 64.35; H, 6.20; N, 3.74.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl-2-oxa-3-azabicyclo[2.2.2]oct-5-en-3-ylmethanone (24a,b)

Yield: 3.84 g (quant.); yellowish oil.

IR (Nujol): 1670 (C=O) cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.30 (m, 5 H_{arom}), 6.62 and 6.50 (m, 1 H + 1 H, CH=CH), 6.09 (d, *J* = 2 Hz, 1 H, OCHO), 5.34 (br s, 1 H, CHO), 4.80 (d, *J* = 2 Hz, 1 H, CHO), 4.74 (br s, 1 H, CHN), 4.62 (d, *J* = 2 Hz, 1 H, CHO), 4.72 and 4.55 (AB syst, 1 H + 1 H, CH_2Ph), 4.36 (d, *J* = 2 Hz, 1 H, CHO), 2.19 and 2.00 (m, 2 H + 2 H, CH_2CH_2), 1.46 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$, 300 MHz): δ = 171.0 (C=O), 137.1, 135.9, 132.4, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.5, 127.4 (arom), 112.4, 112.2, 105.7, 105.5 (CH=CH), 105.3 (OCO), 82.7, 82.5, 82.0, 80.3, 75.1, 72.1 (CHO, CHN), 48.3, 28.8 (CH_2), 26.3, 26.2 (CH_3).

Anal. Calcd for $C_{21}H_{25}NO_6$ (387.43): C, 65.10; H, 6.50; N, 3.62. Found: C, 65.11; H, 6.49; N, 3.64.

Ene Reactions of (3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole-5-carbimidoyl Chloride (22) with Olefins a–g; General Procedure

To a DCM solution (150 mL) of the corresponding olefin **a–g** (15 mmol, 15 equiv) were added NMO (1.41 g, 12 mmol, 1.2 equiv) and distilled Et_3N (1.11 g, 11 mmol, 1.1 equiv). (3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole-5-carbimidoyl chloride (**22**; 3.28 g, 10 mmol, 1 equiv) was then dissolved in DCM (80 mL) and the solution was added dropwise to the olefin solution under stirring at r.t. The reaction mixtures were left to react for 24 h. After this period of time, the mixtures were washed with H_2O (2 × 50 mL) and the organic phases were dried (anhyd Na_2SO_4). The residues obtained after the solvent evaporation were submitted to chromatographic separation for isolation and purification of the products.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-(2,3-dimethylbut-3-en-2-yl)-*N*-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole-5-carboxamide (25a)

Yield: 1.37 g (35%); white crystals (benzene/PE); mp 184–185 °C.

IR (Nujol): 3140 (O–H), 1631 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.55 (s, 1 H, OH), 7.31 (m, 5 H_{arom}), 5.93 (d, *J* = 4 Hz, 1 H, OCHO), 4.96 (d, *J* = 4 Hz, 1 H, CHO), 4.74 and 4.73 (s, 1 H + 1 H, =CH_2), 4.63 (t, *J* = 4 Hz, 1 H, CHO), 4.61 and 4.49 (AB syst, 2 H, CH_2Ph), 4.38 (t, *J* = 4 Hz, 1 H, CHO), 1.64 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.27 (s, 6 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 166.8 (C=O), 149.4 (C=), 137.7, 128.0, 127.8, 127.5 (arom), 110.7 (CH_2=), 108.2 (OCO), 104.1, 82.7, 81.5, 79.1, 71.0 (CHO), 64.9 (CH_2O), 26.7, 26.2, 25.1, 24.6, 19.2 (CH_3).

Anal. Calcd for $C_{21}H_{29}NO_6$ (391.46): C, 64.43; H, 7.47; N, 3.58. Found: C, 64.45; H, 7.46; N, 3.54.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-hydroxy-2,2-dimethyl-*N*-(3-methylbut-3-en-2-yl)tetrahydrofuro[2,3-*d*][1,3]dioxole-5-carboxamide (25b), 1st Diastereoisomer

Yield: 2.04 g (54%); white crystals (benzene/PE); mp 175–177 °C.

IR (Nujol): 3110 (O–H), 1619 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.33 (s, 1 H, OH), 7.31 (m, 5 H_{arom}), 5.98 (d, *J* = 4 Hz, 1 H, OCHCO), 5.07 (d, *J* = 4 Hz, 1 H, CHO), 4.94 and 4.91 (s, 1 H + 1 H, =CH_2), 4.86 (q, *J* = 7 Hz, 1 H, CHN), 4.74 (d, *J* = 4 Hz, 1 H, CHO), 4.54 (AB syst, 2 H, PhCH_2), 4.41 (d, *J* = 4 Hz, 1 H, CHO), 1.70 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.17 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 166.9 (C=O), 143.7 (=C), 137.8, 128.1, 127.5 (arom), 112.4 (=CH_2), 110.9 (OCO), 104.3 (CHO), 82.6, 81.7, 78.6, 71.1 (CHO, CH_2Ph), 54.3 (CHN), 26.8, 26.2, 20.7, 14.5 (CH_3).

Anal. Calcd for $C_{20}H_{27}NO_6$ (377.44): C, 63.65; H, 7.21; N, 3.71. Found: C, 63.65; H, 7.23; N, 3.69.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-hydroxy-2,2-dimethyl-*N*-(3-methylbut-3-en-2-yl)tetrahydrofuro[2,3-*d*][1,3]dioxole-5-carboxamide (25b), 2nd Diastereoisomer

Yield: 2.04 g (54%); white crystals (benzene/PE); mp 178–180 °C.

IR (Nujol): 3158 (O–H), 1634 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.42 (s, 1 H, OH), 7.30 (m, 5 H_{arom}), 5.96 (d, *J* = 4 Hz, 1 H, OCHO), 5.07 (d, *J* = 4 Hz, 1 H, CHO), 4.85 (m, 1 H + 1 H + 1 H, =CH_2 and CHN), 4.74 (d, *J* = 4 Hz, 1 H, CHO), 4.54 (AB syst, 2 H, PhCH_2), 4.41 (d, *J* = 4 Hz, 1 H, CHO), 1.59 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.21 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 166.0 (C=O), 143.9 (=C), 137.7, 128.1, 127.6, 127.4 (arom), 112.2 (=CH_2), 110.8 (OCO), 104.1 (CHO), 82.5, 81.4, 78.3, 70.8 (CHO, CH_2Ph), 54.2 (CHN), 26.8, 26.2, 20.6, 14.7 (CH_3).

Anal. Calcd for $C_{20}H_{27}NO_6$ (377.44): C, 63.65; H, 7.21; N, 3.71. Found: C, 63.67; H, 7.20; N, 3.70.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-(cyclohex-2-en-1-yl)-*N*-hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxole-5-carboxamide (25d), Mixture of Diastereoisomers

Yield: 1.29 g (33%); white crystals (benzene/PE); mp 192–194 °C.

IR (Nujol): 3158 (O–H), 1639 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.51 [9.46] (s, 1 H, OH), 7.32 (m, 5 H_{arom}), 5.98 (d, *J* = 4 Hz, 1 H, OCHCO), 5.91 and 5.49 (m, 1 H + 1 H, CH=CH), 5.02 (d, *J* = 4 Hz, 1 H, CHO), 4.87 (m, 1 H, CHN), 4.71 (d, *J* = 4 Hz, 1 H, CHO), 4.54 (AB syst, 2 H, PhCH_2), 4.38 (d, *J* = 4 Hz, 1 H, CHO), 2.00–1.50 (m, 6 H, CH_2), 1.41 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 166.8, [166.7] (C=O), 137.8, [137.7], 131.2, [130.6], 128.1, 127.6, 127.5, 127.4, 126.9, 126.8 (arom), 110.9 (CH=CH), 104.3 (OCO), 82.6, [82.5] (CHN), 81.9, [81.7], 78.7, [78.6], 71.2 (CHO), 51.7 (CH_2), 26.8, 26.2, 25.3, [25.1], 23.9, 20.7, [20.5] (CH_3).

Anal. Calcd for $C_{22}H_{27}NO_6$ (389.45): C, 64.77; H, 6.99; N, 3.60. Found: C, 64.75; H, 7.01; N, 3.60.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-hydroxy-2,2-dimethyl-*N*-(2-phenylallyl)tetrahydrofuro[2,3-*d*][1,3]dioxole-5-carboxamide (25e)

Yield: 1.71 g (44%); white crystals (benzene/PE); mp 195–196 °C.

IR (Nujol): 3152 (O–H), 1624 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.86 (s, 1 H, OH), 7.53 (d, *J* = 7 Hz, 2 H_{arom}) 7.30 (m, 8 H_{arom}), 5.98 (d, *J* = 4 Hz, 1 H, OCHCO), 5.61 and 5.29 (s, 1 H + 1 H, =CH_2), 5.06 (d, *J* = 4 Hz, 1 H, C*H*OBn), 4.73 (d, *J* = 4 Hz, 1 H, CHO), 4.65 (AB syst, 2 H, CH_2N), 4.50 (AB syst, 2 H, PhCH_2), 4.38 (d, *J* = 4 Hz, 1 H, CHO), 1.40 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 167.0 (C=O), 141.0 (=C), 137.9, 137.7, 128.4, 128.1, 127.8, 127.6, 127.5, 125.7 (arom), 115.3 (=CH_2), 110.9 (OCO), 104.3 (CHO), 82.4, 81.8, 78.4, 71.0 (CHO, CH_2Ph), 51.5 (CHN), 26.7, 26.2 (CH_3).

Anal. Calcd for $C_{22}H_{27}NO_6$ (389.45): C, 64.77; H, 6.99; N, 3.60. Found: C, 64.75; H, 7.01; N, 3.60.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-hydroxy-2,2-dimethyl-*N*-[(*E*)-3-methylpent-3-en-2-yl]tetrahydrofuro[2,3-*d*][1,3]dioxole-5-carboxamide (25f), Mixture of Diastereoisomers

Yield: 1.17 g (30%); white crystals (benzene/PE); mp 180–182 °C.

IR (Nujol): 3149 (O–H), 1626 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.34 [9.36] (s, 1 H, OH), 7.30 (m, 5 H_{arom}), 5.96 [5.95] (d, *J* = 4 Hz, 1 H, OCHO), 5.01 (d, *J* = 4 Hz, 1 H, CHO), 4.94 and 4.87 (s, 1 H + 1 H, =CH_2), 4.94 (1 H, CHN), 4.77 (d, *J* = 4 Hz, 1 H, CHO), 4.52 (AB syst, 2 H, PhCH_2), 4.38 (d, *J* = 4 Hz, 1 H, CHO), 1.90 (m, 2 H, CH_2), 1.48 [1.41] (s, 3 H, CH_3), 1.28 [1.25] (s, 3 H, CH_3), 1.22 [1.20] (d, *J* = 7 Hz, 3 H, CH_3), 0.76 [0.75] (t, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 165.7 [164.6] (C=O), 148.5 (=C), 133.8, 129.2, 128.9, 128.8, 128.1, 127.6 (arom), 111.3 [110.5] (=CH), 104.3 (OC), 82.7, 77.2, 77.0 (CHO, CH_2Ph), 53.0 (CHN), 26.6, 26.3, 26.2, 14.4, 11.9 (CH_3).

Anal. Calcd for $C_{21}H_{29}NO_6$ (391.46): C, 64.43; H, 7.47; N, 3.58. Found: C, 64.45; H, 7.50; N, 3.58.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-hydroxy-2,2-dimethyl-*N*-(3-methylenepentan-2-yl)tetrahydrofuro[2,3-*d*][1,3]dioxole-5-carboxamide (25g), 1st Diastereoisomer

Yield: 1.80 g (46%); white crystals (benzene/PE); mp 178–179 °C.

IR (Nujol): 3134 (O–H), 1640 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.27 (s, 1 H, OH), 7.32 (m, 5 H_{arom}), 5.98 (d, *J* = 4 Hz, 1 H, OCHCO), 5.05 (d, *J* = 4 Hz, 1 H, C*H*OBn), 4.95 (s, 2 H, =CH_2), 4.92 (q, *J* = 7 Hz, 1 H, CHN), 4.74 (d, *J* = 4 Hz, 1 H, CHO), 4.55 (AB syst, 2 H, PhCH_2), 4.39 (d, *J* = 4 Hz, 1 H, CHO), 1.99 (m, 2 H, CH_2), 1.41 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.17 (d, *J* = 7 Hz, 3 H, CH_3), 0.99 (t, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 166.8 (C=O), 149.0 (=C), 137.7, 128.1, 127.5 (arom), 110.8 (=CH_2), 110.3 (OCO), 104.3 (CHO), 82.6, 81.7, 78.5, 71.1 (CHO, *C*H_2Ph), 52.8 (CHN), 26.8, 26.3, 26.2, 14.6, 12.0 (CH_2 and CH_3).

Anal. Calcd for $C_{21}H_{29}NO_6$ (391.46): C, 64.43; H, 7.47; N, 3.58. Found: C, 64.42; H, 7.49; N, 3.59.

(3a*R*,5*S*,6*R*,6a*R*)-6-(Benzyloxy)-*N*-hydroxy-2,2-dimethyl-*N*-(3-methylenepentan-2-yl)tetrahydrofuro[2,3-*d*][1,3]dioxole-5-carboxamide (25g), 2nd Diastereoisomer

Yield: 1.80 g (46%); white crystals (benzene/PE); mp 185–186 °C.

IR (Nujol): 3176 (O–H), 1628 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.36 (s, 1 H, OH), 7.30 (m, 5 H_{arom}), 5.95 (d, *J* = 4 Hz, 1 H, OCHO), 5.05 (d, *J* = 4 Hz, 1 H, CHO), 4.92 and 4.89 (s, 1 H + 1 H, =CH_2), 4.95 (m, 1 H, CHN), 4.75 (d, *J* = 4 Hz, 1 H, CHO), 4.53 (AB syst, 2 H, PhCH_2), 4.36 (d, *J* = 4 Hz, 1 H, CHO), 1.90 (m, 2 H, CH_2), 1.42 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.23 (d, *J* = 7 Hz, 3 H, CH_3), 0.78 (t, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 166.0 (C=O), 149.4 (=C), 137.7, 128.1, 128.0, 127.5, 127.4, 127.3 (arom), 110.8 (=CH_2), 110.0 (OCO), 104.1 (CHO), 82.4, 81.4, 78.4, 70.7 (CHO, *C*H_2Ph), 52.7 (CHN), 26.7, 26.1, 14.8, 11.8 (CH_2 and CH_3).

Anal. Calcd for $C_{21}H_{29}NO_6$ (391.46): C, 64.43; H, 7.47; N, 3.58. Found: C, 64.42; H, 7.49; N, 3.59.

(3a*R*,5*S*,6*R*,6a*R*)-5-[(2,3-Dimethylbut-3-en-2-yl)(hydroxy)carbamoyl]-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl Benzoate (26a)

Yield: 1.34 g (33%); white crystals (benzene/PE); mp 208–209 °C.

IR (Nujol): 3176 (O–H), 1721 (C=O, ester), 1638 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.71 (s, 1 H, OH), 7.89 (m, 2 H_{arom}), 7.67 (m, 1 H_{arom}), 7.53 (m, 2 H_{arom}) 6.02 (d, *J* = 4 Hz, 1 H, OCHO), 5.58 (d, *J* = 3 Hz, 1 H, CHO), 5.15 (d, *J* = 4 Hz, 1 H, CHO), 4.71 (s, 2 H, =CH_2), 4.58 (s, 1 H, CHO), 1.53 (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.24 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 165.6, 164.6 (C=O), 148.9 (C=), 133.8, 129.4, 128.9, 128.6 (arom), 111.2 (CH_2=), 108.5 (OCO), 104.1, 82.6, 77.5, 77.4, 65.0 (CHO, CN), 26.5, 26.1, 25.0, 24.4, 18.9 (CH_3).

Anal. Calcd for $C_{21}H_{27}NO_7$ (405.45): C, 62.21; H, 6.71; N, 3.45. Found: C, 62.22; H, 6.70; N, 3.44.

(3a*R*,5*S*,6*R*,6a*R*)-5-[Hydroxy(3-methylbut-3-en-2-yl)carbamoyl]-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl Benzoate (26b), Mixture of Diastereoisomers

Yield: 0.70 g (18%); white crystals (benzene/PE); mp 200 °C (dec.).

IR (Nujol): 3170 (O–H), 1731 (C=O, ester), 1635 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.49 [9.33] (s, 1 H, OH), 7.90 (m, 2 H_{arom}), 7.68 (m, 1 H_{arom}), 7.54 (m, 2 H_{arom}), 6.08 (d, *J* = 4 Hz, 1 H, OCHO), 5.58 (d, *J* = 4 Hz, 1 H, CHO), 5.24 (d, *J* = 4 Hz, 1 H, CHO), 4.93 and 4.85 (s, 1 H + 1 H, =CH_2), 4.83 (q, *J* = 3 Hz, 1 H, CHN), 4.77 (d, *J* = 4 Hz, 1 H, CHO), 1.69 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 165.8, [164.6] (C=O), [143.6] 143.2 (C=), 137.7, 133.8, 129.2, 128.9, 128.8, 128.1, 127.5 (arom), 112.6, [111.4] (CH=CH), 104.3 (OCO), 82.7, [81.6], [78.5], 77.2, 77.0, [71.1] (CHO), 54.4, [54.3] (CHN), [26.8], 26.6, 26.1, 20.7, [14.5], 14.3 (CH_3).

Anal. Calcd for $C_{20}H_{25}NO_7$ (391.42): C, 61.37; H, 6.44; N, 3.58. Found: C, 61.35; H, 6.41; N, 3.58.

(3a*R*,5*S*,6*R*,6a*R*)-5-[Cyclopent-2-en-1-yl(hydroxy)carbamoyl]-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl Benzoate (26c), Mixture of Diastereoisomers

Yield: 1.25 g (32%); white crystals (benzene/PE); mp 225 °C (dec.).

IR (Nujol: 3164 (O–H), 1725 (C=O, ester), 1635 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.57 [9.53] (s, 1 H, OH), 7.90 (m, 2 H_{arom}), 7.69 (m, 1 H_{arom}), 7.54 (m, 2 H_{arom}), 6.09 (m, 1 H, OCHO), 5.99 and 5.83 (m, 1 H + 1 H, CH=CH), 5.53 (d, *J* = 4 Hz, 1 H, CHO), 5.19 (t, *J* = 4 Hz, 1 H, CHO), 5.39 (m, 1 H, CHN), 4.77 (t, *J* = 4 Hz, 1 H, CHO), 2.40–1.60 (m, 4 H, CH_2), 1.47 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 165.0, [164.2] (C=O), 133.9, 133.4, 128.9, 128.6, 128.4, 128.1, 127.6, 127.1 (arom), 111.0 (CH=CH), 104.0 (OCO), 82.2, 76.9, 76.8 (CHO), 61.0 (CH_2O), 30.8, 26.2, 25.8, 24.9 (CH_2 and CH_3).

Anal. Calcd for $C_{20}H_{23}NO_7$ (389.40): C, 61.69; H, 5.95; N, 3.60. Found: C, 61.68; H, 5.93; N, 3.58.

(3a*R*,5*S*,6*R*,6a*R*)-5-{Hydroxy[(*E*)-3-methylpent-3-en-2-yl]carbamoyl}-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl Benzoate (26f), Mixture of Diastereoisomers

Yield: 0.73 g (18%); white crystals (benzene/PE); mp 209–210 °C.

IR (Nujol): 3086 (O–H), 1724 (C=O, ester), 1632 (C=O) cm^{-1}.

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 9.36 (s, 1 H, OH), 7.89 (m, 2 H_{arom}), 7.68 (m, 1 H_{arom}), 7.54 (m, 2 H_{arom}), 6.07 (d, *J* = 4 Hz, 1 H, OCHO), 5.57 (d, *J* = 3 Hz, 1 H, CHO), 5.35 (q, *J* = 3 Hz, 1 H, =CH), 5.21 (d, *J* = 4 Hz, 1 H, CHO), 4.80 (q, *J* = 6 Hz, 1 H, CHN), 4.75 (d, *J* = 4 Hz, 1 H, CHO), 1.58 (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 0.90 (d, *J* = 7 Hz, 3 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 165.5, [164.6] (C=O), 133.8, [133.7], 129.2, 128.9, 128.7, 128.1, 127.5 (arom), 120.4 (=CH), 111.3 (OCO), 104.3, 82.7, 77.2, 77.0 (CHO), 55.6 (CHN), 26.6, [26.2], 14.3, [14.2], 13.2 (CH_3).

Anal. Calcd for $C_{21}H_{27}NO_7$ (405.45): C, 62.21; H, 6.71; N, 3.45. Found: C, 62.22; H, 6.73; N, 3.43.

(3a*R*,5*S*,6*R*,6a*R*)-5-[Hydroxy(3-methylenepentan-2-yl)carbamoyl]-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl Benzoate (26g), Mixture of Diastereoisomers

Yield: 0.69 g (17%); white crystals (benzene/PE); mp 196–197 °C.

IR (Nujol): 3116 (O–H), 1725 (C=O, ester), 1637 (C=O) cm^{-1}.

^1H NMR (DMSO-d_6, 300 MHz): δ = 9.43 (s, 1 H, OH), 7.89 (m, 2 H_{arom}), 7.67 (m, 1 H_{arom}), 7.53 (m, 2 H_{arom}), 6.06 (d, *J* = 4 Hz, 1 H, OCHO), 5.58 (d, *J* = 4 Hz, 1 H, CHO), 5.22 (d, *J* = 4 Hz, 1 H, CHO), 4.92 and 4.89 (s, 1 H + 1 H, =CH_2), 4.94 (q, *J* = 8 Hz, 1 H, CHN), 4.75 (d, *J* = 4 Hz, 1 H, CHO), 1.99 (m, 2 H, CH_2), 1.47 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 0.96 (m, 6 H, CH_3).

^{13}C NMR (DMSO-d_6, 300 MHz): δ = 165.7, [164.6] (C=O), 148.5 (C=), 133.8, 129.2, 128.9, 128.1, 127.6 (arom), 111.4 (=CH_2), 110.5 (OCO), 104.3, 82.7, 77.2, 77.0 (CHO), 53.0 (CHN), 26.6, 26.3, 26.2, 14.4, 11.9 (CH_3).

Anal. Calcd for $C_{21}H_{27}NO_7$ (405.45): C, 62.21; H, 6.71; N, 3.45. Found: C, 62.20; H, 6.72; N, 3.45.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1707276.

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